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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/575,061	05/19/2000	STEPHAN R. TARGAN	P-PM 4097	1578

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EXAMINER	
GABEL, GAILENE	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 01/07/2003 20

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/575,061	TARGAN ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *8-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-11* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/9/02 has been entered.

Amendment Entry

2. Applicant's amendment and response filed 11/25/02 in Paper No. 19 is acknowledged and has been entered. Claims 12 and 13 have been cancelled. Claim 2 has been amended. Accordingly, claims 1-11 are pending. Claims 1-7 are under examination.

Rejections Withdrawn

3. In light of Applicant's amendment and arguments, the rejection of claims 2-7 under 35 U.S.C. 112, second paragraph, is hereby, withdrawn.

4. In light of Applicant's amendment and arguments, the rejection of claims 1-4 under 35 U.S.C. 102(e) as being anticipated by Braun et al. (US 6,033,864) is hereby, withdrawn.

5. In light of Applicant's amendment and arguments, the rejection of claims 5-7 under 35 U.S.C. 103(a) as being unpatentable over Braun et al. (US 6,033,864) in view of Targan et al. (US 5,932,429) is hereby, withdrawn.

New Grounds of Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for all of IgA outer membrane porin C (OmpC) antibody as a diagnostic marker detected using OmpC antigen, anti-Saccharomyces cerevisiae antibody (ASCA), I-2 polypeptide antibody (I-2), and perinuclear anti-neutrophil antibodies (pANCA) as a diagnostic system to diagnose the presence of Crohn's disease, does not reasonably provide enablement for each one of IgA OmpC antibody detected using OmpC antigen or fragment thereof, ASCA, I-2 polypeptide antibody, and pANCA to, independently and individually, diagnose the presence of Crohn's disease (CD). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As set forth in In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), enablement requires that the specification teach those skilled in the art to make and use

the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The nature of the invention- the invention is directed to a method of diagnosing CD in a subject by determining the presence of IgA OmpC antibody in the subject using OmpC antigen, ASCA, I-2 polypeptide antibody, and pANCA, wherein the presence of all of IgA OmpC, ASCA, I-2 antibody, and pANCA antibody in a diagnostic system, is diagnostic of the presence of CD in the subject.

The state of the prior art- the prior art of record fails to disclose a method of diagnosing CD by determining the presence of IgA OmpC antibody in the subject using OmpC antigen, wherein the presence of IgA OmpC antibody is diagnostic of the presence of CD in the subject.

The predictability or lack thereof in the art- there is no predictability based on the instant specification that the claimed method will work for diagnosing the presence of CD using IgA OmpC antibody using OmpC antigenic reactive fragments, alone, and without combination with ASCA, I-2 antibody, and pANCA in a diagnostic system.

The amount of direction or guidance present- appropriate guidance is provided by the specification for the claimed method to work using a diagnostic system

comprising IgA OmpC antibody detected using OmpC antigen, ASCA, I-2 antibody, and pANCA in diagnosing the presence of CD in a subject.

The presence or absence of working examples- working examples are provided in the specification that show diagnosis of CD using a diagnostic system comprising IgA OmpC detected using OmpC antigen, ASCA, I-2 antibody, and pANCA for diagnosing the presence of CD in a subject. There are no working examples that show analogous results using each one of IgA OmpC detected using OmpC antigen, ASCA, I-2 antibody, and pANCA, individually and independently, for diagnosing the presence of CD.

The quantity of experimentation necessary- it would require undue amount of experimentation for the skilled artisan to make and use the method as claimed.

The relative skill of those in the art-the level of skill in the art is high.

The breadth of the claims- as recited, the instant claims are directed to a method of diagnosing CD in a subject by determining the presence of IgA OmpC antibody using OmpC antigen or a reactive fragment thereof, wherein the presence of IgA OmpC or ASCA or I-2 antibody, is individually and independently, diagnostic of the presence of CD in the subject.

(1) With respect to the reactive fragment of OmpC antigen, the specification only provides that the reactive fragment or tolerogenic fragment of an OmpC antigen can be a peptide mimetic which retains preferential reactivity with IgA antibodies of CD patients and can be produced or synthesized using methods well known in the art, i.e. DNA, chemical synthesis (pages 13-15). At pages 28-29, the specification shows ways of identifying OmpC antigen such as by screening of a library of peptides of interest and

such a panel of peptides may span the sequence of the OmpC antigen SEQ ID No. 1, each overlapping by three to five residue shifts or having one or more amino acids that differ from SEQ ID No. 1. However; the specification fails to provide adequate description for the claimed reactive fragments of OmpC because it does not disclose representative species of fragments and analogs described by structure, physical or chemical characteristics, function correlated with structure, or a combination of each aforementioned, sufficient to establish that the applicant had possession of the claimed reactive fragments and analogs. See the Interim Guidelines on Written Description (Fed Reg , June 15, 1998, Volume 63, Number 114, pages 32639-32645). The instant specification does not contain supportive description of each reactive fragment of OmpC for use in a method of detecting IgA OmpC antibody wherein the presence of IgA OmpC antibody is diagnostic of the presence of CD, in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing. Adequate description requires more than a mere statement of requisite use of reactive fragments of OmpC as part of the invention and a reference to a potential method of making it. The nuclei acid itself is required. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016.

The claimed OmpC recites a genus claim encompassing SEQ ID No. 1, which while being enabling in and of itself, is not enabled for species drawn to reactive fragments and analogs of OmpC structure, having a specific reactive site for use in a method of diagnosing CD as required within the scope of the claimed invention. A

representative number of species have not been described or defined by sufficient relevant identifying characteristics, such as function correlated with structural characteristics. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Thus, the claimed method is only enabled for OmpC antigen having SEQ ID No. 1 for use in binding with IgA OmpC antibody in a subject for diagnosing CD.

With regards to diagnosing the presence of CD, while the specification provides that IgA OmpC antibody using OmpC antigen can be contributory to the diagnosis of CD using the claimed assay method (page 3), the specification does not show any working examples of the claimed method using only IgA OmpC antibody as a sole diagnostic marker of CD. The fact that the claimed method appears to work in identifying 55% of patients having CD is not sufficient to enable the breadth of the claimed method for using IgA OmpC as a sole diagnostic marker of CD in patients. The specification does not establish a direct correlation which would lead the skilled artisan to say that if the claimed method works in 55% of CD patients, then it should work in all patients having CD, to enable the breadth of the claimed method. The specification does not provide any teaching that suggests and supports that IgA OmpC antibody can be considered a sole diagnostic marker for CD. Page 6, Table 1, and Figures 1 and 2 of the specification discloses that IgA OmpC antibody in addition or combination to ASCA, I-2 polypeptide antibody, and pANCA provides a highly sensitive diagnostic system which can detect 86% of patients with CD but provides no showing that the claimed method works in using only IgA OmpC antibody. Table 2 shows that IgA OmpC reactivity

detected only 55% of patients having CD. Additionally, ASCA, I-2 polypeptide antibody, and pANCA show detection capability of 56%, 52%, and 24% only, respectively, individually and independently. While it is not necessary to show working examples for every possible embodiment, there should be sufficient teachings in the specification that would suggest to the skilled artisan that the breadth of the claimed method is enabled. This is not the case in the instant specification. Thus, the claimed method is only enabled for a diagnostic system comprising IgA OmpC antibody, ASCA, I-2 polypeptide antibody, and pANCA as combined diagnostic markers in diagnosing the presence of CD.

In view of the teachings of In re Wands, 8 USPQ2d 1400, it has been determined that the level of experimentation required to enable the breadth of the claims is undue. It has been set forth above that 1) the experimentation required to enable the claimed method for diagnosing CD using only IgA OmpC antibody as a diagnostic marker, would be great as 2) there is no experimental evidence provided that would indicate that the claimed method would work in greater than 56% of CD patients; 3) there is no proper guidance that shows that IgA OmpC antibody is an acceptable sole diagnostic marker for diagnosing the presence of CD, 4) the nature of the invention is a method of diagnosing CD in a subject by determining the presence of IgA OmpC antibody in the subject using OmpC antigen, ASCA, I-2 antibody, and pANCA, wherein the presence of all of IgA OmpC, ASCA, I-2 antibody, and pANCA antibody in a diagnostic system, is effective in diagnosing the presence of CD in a subject, 5) the relative skill of those in the art is high, yet 6) the state of the prior art has been shown to be unpredictable as

evidenced by the fact that no prior art has been cited that shows that the claimed method will work for diagnosing the presence of CD in all patients using IgA OmpC antibody, alone, and without combination with ASCA, I-2 antibody, and pANCA in a diagnostic system, and lastly 7) the claims broadly recite a method of diagnosing CD in a subject by determining the presence of IgA OmpC antibody using OmpC antigen or a reactive fragment thereof, wherein the presence of IgA OmpC or ASCA or I-2 antibody, is individually and independently, diagnostic of the presence of CD in the subject.

Therefore, it is maintained that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

Response to Arguments

7. Applicant's arguments filed 2/8/02 have been fully considered but they are not persuasive.

A) Applicant requests rejoinder of claims 8-11 because while claims 8 and 10 require determination of other antibodies using other antigens, these claims also require determining the presence or absence of IgA anti-OmpC antibodies as in elected claims 1-7.

In response, it is maintained that claims 8-11 are drawn to distinct and independent inventions because of the use of distinct markers in combination with IgA OmpC antibody in diagnosing Crohn's Disease.

I. Claims 1-7 use IgA OmpC antibody and IgA ASCA as diagnostic markers of Crohn's disease.

II. Claims 8-9 use IgA OmpC antibody and IgA anti-I-2 polypeptide antibodies as diagnostic markers of Crohn's disease

III. Claims 10-11 use IgA OmpC antibody, IgA ASCA, and IgA anti-I-2 polypeptide antibodies as combined diagnostic markers of Crohn's disease.

Accordingly, literature search for each method is distinct since the structural requirements of each of the three inventions are different. While searches would be expected to overlap, there is no reason to expect the searches to be coextensive.

8. Applicant's arguments with respect to claims 1-7 have been considered but are moot in view of the new grounds of rejection. Accordingly, no claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday, 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
December 27, 2002

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

12/29/02